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Palladium-catalyzed annulation reactions of methyl *o*-halobenzoates with azabicyclic alkenes: a general protocol for the construction of benzo[*c*]phenanthridine derivatives†

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The annulation reaction of methyl *o*-halobenzoates with azabicyclic alkenes proceeds efficiently to give the corresponding benzo[*c*]phenanthridine derivatives in good to excellent yields using a developed base-free methodology based on our preliminary studies. Thirty-seven application examples validate the compatibility of the present strategy with different groups, particularly with the electron-deficient ones, that are difficult to access using other traditional methods. In addition, annulation reactions with non-symmetric azabicyclic alkenes are achieved in high regioselectivity.

Introduction

Benzo[*c*]phenanthridines (Fig. 1) are naturally occurring alkaloids widely distributed in the plants of the Papaveraceae and Rutaceae families with a long history,[1] dating back to their initial discovery in 1839.[2] By reviewing a considerable amount of relevant literature, we learned that the majority of these alkaloids can mediate various biological properties.[3] Sanguinarine, which belongs to a fully aromatized-type alkaloid, exhibits antibacterial[4] and antifungal[5] activities, whereas nitidine and fagaronine have been investigated for being potential anti-tumor[6] and antimalarial[7] agents. Chelidonine, a B/C-*cis*-hexahydro-type alkaloid representative that indicates a wide range of pharmacological activities as well, has been used successfully in experimental oncology.[8] Over the last decades, syntheses of these natural products have been an area of great interest for synthetic chemists, thereby spurring the rapid development of efficient construction for a benzo[*c*]phenanthridine skeleton.[9] However, some of these previously reported benzo[*c*]phenanthridine synthetic studies involved multi-step sequences and lacked of generality needed for these methods to be applied in the pharmaceutical industry. In addition, an in-depth analysis on the National Cancer Institute preliminary studies showed that the development of several natural products of this family as pharmaceuticals failed to be pursued because of its toxicity and instability.[10] Thus, the development of new and accessible synthetic pathways of benzo[*c*]phenanthridine derivatives and alkaloids in this family is increasingly becoming the primary focus of heterocyclic chemistry. Such developments aim to solve the toxicological or instability problems that accompany some of the naturally occurring alkaloids and to find new target molecules.[11] For example, the synthesis and study of the biological activities of cytostatically active aminodihydro benzo[*c*]phenanthridines and NK109 derivatives have been achieved by Clement[12] and Nakanishi,[13] respectively. Substitutes of the natural benzo[*c*]phenanthridine nucleus and their synthesizing analogues are almost electron-donating groups similar to the alkoxy group, whereas a few electron-deficient groups such as fluorine exist in this family.[14] This information may explain the low cytotoxic activity of some analogues and the failure of the anti-tumor preclinical trials of these natural substances. Consequently, a general and convergent route to construct varieties of benzo[*c*]phenanthri-

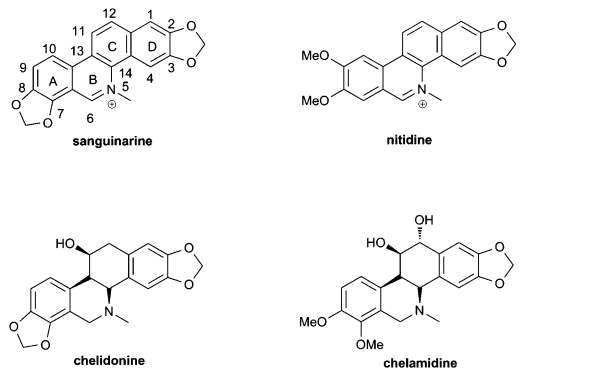

Fig. 1 Naturally occuring benzo[c]phenanthridine alkaloids.

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dines bearing either electron-donating or electron-withdrawing groups is highly necessary.

The palladium-catalyzed ring opening of *meso* heterobicyclic alkenes, conceived by Lautens, Martin and others, constitutes an interesting concept in opening new routes to complex fused ring systems.[15] Driven by these findings, a facile and general method for constructing the ring system of benzo[*c*]phenanthridine alkaloids *via* palladium-mediated annulation reactions of azabicyclic alkene with methyl *o*-iodobenzoates has been reported by our laboratory and applied in the total synthesis of four typical benzo[*c*]phenanthridine alkaloids.[16] In these annulation reactions, electron-rich substrates generally produced satisfactory yields. However, the yields were extraordinarily poor when electron-deficient coupling substrates were tested. Based on these initial results, we further studied various electron-deficient methyl *o*-iodobenzoates to ascertain the scope of tolerance of its substituent in this annulation reaction and a base-free methodology was developed. This paper reports the successful improvement of our developed protocol for the construction of benzo[*c*]phenanthridine nucleus using methyl *o*-halobenzoates as coupling substrates with azabicyclic alkenes.

Results and discussion

As a starting point, we chose methyl 4-fluoro-2-iodobenzoate **1a** as the representative electron-deficient substrate to couple with azabicyclic alkene **2a**[17] under standard conditions of $PdCl_2(PPh_3)_2$-Zn-$ZnCl_2$-Et_3N-THF at 60 °C for 24 h[15] (Table 1, entry 1). However, the target product in relative configuration was obtained only in 14% yield, which was improved to 35% upon raising the reaction temperature from 60 °C to 65 °C. The conversion of the starting materials was incomplete, and two by-products **4aa** and **5aa** (Fig. 2) were isolated as a result of an unexpected double-bond migration. These two by-products,

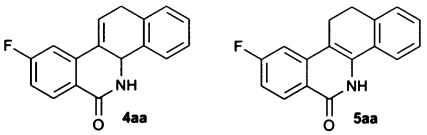


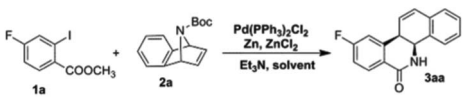
Fig. 2 Structures of the two by-products.

whose structures were fully characterized by ^1H and ^{13}C NMR and HRMS, significantly decreased the efficacy of the reaction.

Control experiments revealed that no reaction occurred in the absence of palladium complexes and zinc powder or zinc chloride. However, without the addition of triethylamine as a base, the rearrangement was unexpectedly suppressed (Table 1, entries 1 and 2). Previous studies of this catalytic reaction show that the polarity of the utilized solvents plays an important role in the coupling of iodo esters with azabicycle. Therefore, the solvents were extensively screened and the results are indicated in Table 1. THF, acetonitrile, and toluene were all inferior to 1,4-dioxane as a solvent. This coupling reaction did not proceed in DMF (Table 1, entry 7). In addition, the impacts of triethylamine to these solvents during the reaction were also compared. For instance, heating in toluene at 100 °C for 1 h produced a large amount of rearranged products, yet a minimal amount of the expected product was obtained. By contrast, 40% yield of product was isolated when triethylamine was not involved (Table 1, entry 4). Although the exact pathway of this annulation reaction is not very clear, this unexpected finding may be helpful for further investigation on the reaction mechanism. The desired product was finally obtained in 1,4-dioxane at 100 °C with a satisfactory yield of 93% in only one hour (Table 1, entry 5).

The scope of various substituted methyl *o*-iodobenzoates with azabicyclic alkene **2a** was investigated under optimal reaction conditions and the results are summarized in Table 2. All annulation reactions efficiently gave excellent yields under the present reaction conditions. The trifluoromethyl-substituted dihydrobenzo[*c*]phenanthridin-6-one **3al** was obtained in 90% yield using this catalyst system (Table 2, entry 11). The amino substituted product **3an** and *N*,*N*-dimethyl substituted analogues **3ao** were also obtained by this method (Table 2, entries 13 and 14). All substrates with electron-donating groups underwent efficient annulation reactions and resulted in excellent yields (Table 2, entries 6, 7, and 8). Coupling with a nitro-substituted substrate resulted in the same product as the amino substitute, perhaps because the nitro group was reduced by zinc powder in this reaction (Table 2, entry 16, 90% and entry 13, 91%). These data showed that the electron properties of the methyl *o*-iodobenzoates did not significantly influence the efficacy of the annulation reaction. Steric effects seemed important, as 3-substituted methyl *o*-iodobenzoates reacted in reduced yield (Table 2, entry 1, 75%; 4, 71%; and entry 12, 71%). All reactions were generally completed within 1 h with the exception of methyl 5-bromo-2-iodobenzoate (Table 2, entry 9). Monitored by TLC, the corresponding

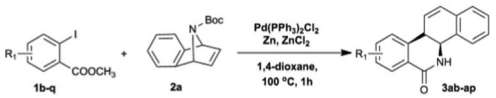
Table 1 Optimization of the reaction conditions of methyl 4-fluoro-2-iodobenzoate **1a** with azabicycle **2a**[a]



Entry	Solvent	*T*/°C	Time (h)	Yield (%)[b]	Yield (%)[c]
1	THF	60	24	14	20
2	THF	65	24	35	45
3	CH_3CN	80	24	56	70
4	Toluene	100	1	trace	40
5	1,4-dioxane	100	1	76	93
6	1,4-dioxane	60	10	63	87
7	DMF	100	1	NR	NR

[a] Reaction conditions: $Pd(PPh_3)_2Cl_2$ (5% mmol), **1a** (1.0 mmol), **2a** (1.1 equiv), Zn (10 equiv), Et_3N (8 equiv), solvent (10 ml), $ZnCl_2$ (0.5 equiv). [b] Yield of isolated product. [c] Isolated yield without Et_3N NR: no reaction.

Table 2 Scope of the annulation reactions of methyl *o*-iodobenzoates **1** with azabicycle **2a**[a]



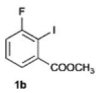
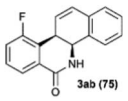
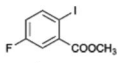
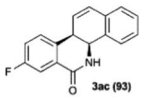
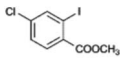
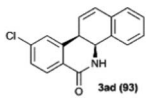
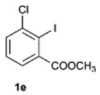
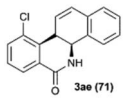
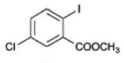
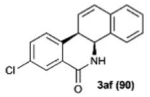
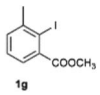
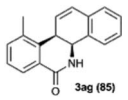
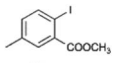
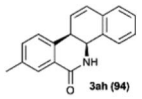
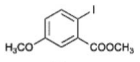
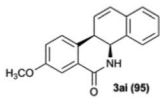
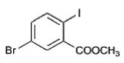
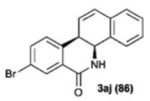
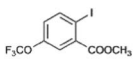
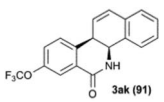
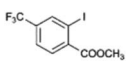
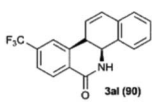
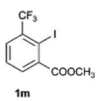
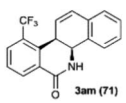
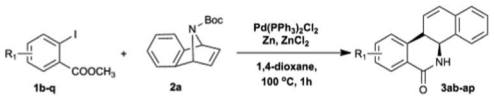
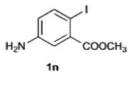
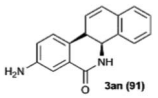
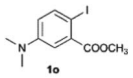
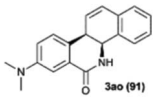
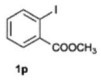
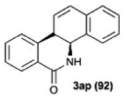
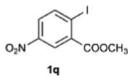
Entry	Methyl *o*-iodobenzoate	Product (yield %)[b]
1	 1b	 3ab (75)
2	 1c	 3ac (93)
3	 1d	 3ad (93)
4	 1e	 3ae (71)
5	 1f	 3af (90)
6	 1g	 3ag (85)
7	 1h	 3ah (94)
8	 1i	 3ai (95)
9[c]	 1j	 3aj (86)
10	 1k	 3ak (91)
11	 1l	 3al (90)
12	 1m	 3am (71)

Table 2 (*Continued*)



Entry	Methyl *o*-iodobenzoate	Product (yield %)[b]
13	 1n	 3an (91)
14	 1o	 3ao (91)
15	 1p	 3ap (92)
16	 1q	**3an** (90)

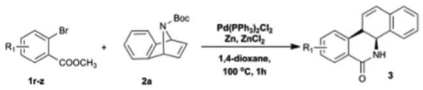
[a] Unless otherwise stated, all reactions were carried out under the optimized conditions mentioned above. [b] Isolated yields. [c] Reaction temperature and time for entry 9 was 60 °C and 10 h, respectively.

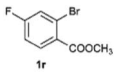
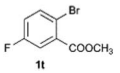
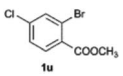
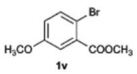
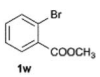
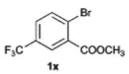
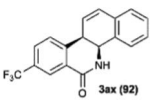
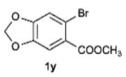
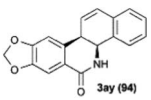
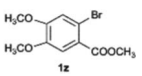
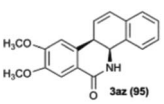
product **3aj** was ultimately obtained at 60 °C after 10 h with an isolated yield of 86%.

These results prompted us to examine this reaction using the corresponding substituted methyl *o*-bromobenzoates under the optimal conditions, which provided almost the same result as the methyl *o*-iodobenzoates (Table 3). Undoubtedly, this unexpected finding broadened the scope of the application of this catalytic reaction because most bromo species are commercially available and stable compared with the iodo counterparts.

Considering that most of the natural benzo[*c*]phenanthridines bear the 1,3-benzodioxole moiety, 1,3-benzodioxole-azabicycle **2b**[18] was selected as the coupling partner to ascertain the scope of its group compatibility either with the iodo species or the bromo species. The results are presented in Table 4. To examine the regioselectivity of the present catalytic reaction, the scope and value of this method were further extended by employing two unsymmetrical azabicyclic alkenes, namely **2c**, which bears a methyl group at a bridgehead atom, and **2d**, which comprises two methyl groups (Table 5). The presence of the methyl group on the bridgehead atom of **2c** appears to block the addition of an organic group to the nearby double-bond carbon. In the two substrates, namely, **1a** and **1p**, the organic groups all added to the olefin carbon distal to the methyl group, which gave the corresponding regioselective benzo[*c*]phenanthridines **3ca** and **3cp** in 76% and 71% yield, respectively. These could be readily characterized by the ^{1}H NMR in the presence of a single olefin proton resonance. In contrast to the results observed for **2c**, no reaction occurred

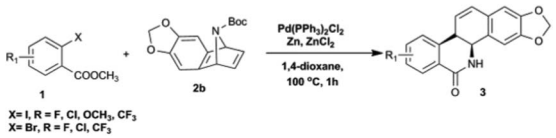
Table 3 Scope of methyl *o*-bromobenzoate component[a]

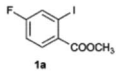
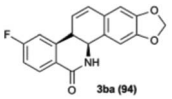
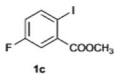
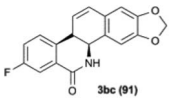
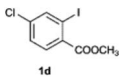
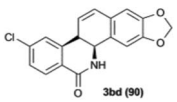
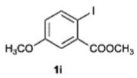
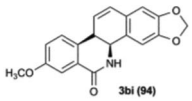
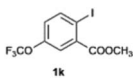
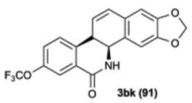
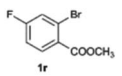
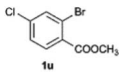
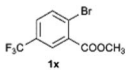
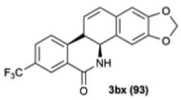


Entry	Methyl *o*-bromobenzoate	Product (yield %)[b]
1	 1r	**3aa** (91)
2	 1s	**3ab** (73)
3	 1t	**3ac** (90)
4	 1u	**3ad** (91)
5	 1v	**3ai** (94)
6	 1w	**3ap** (92)
7	 1x	 3ax (92)
8	 1y	 3ay (94)
9	 1z	 3az (95)

[a] Unless otherwise stated, all reactions were carried out under the optimized conditions mentioned above. [b] Isolated yields.

Table 4 Scope of 1,3-benzodioxole-azabicycle component[a]



Entry	Methyl *o*-halobenzoate	Product (yield %)[b]
1	 1a	 3ba (94)
2	 1c	 3bc (91)
3	 1d	 3bd (90)
4	 1i	 3bi (94)
5	 1k	 3bk (91)
6	 1r	**3ba** (92)
7	 1u	**3bd** (93)
8	 1x	 3bx (93)

[a] Unless otherwise stated, all reactions were carried out under the optimized conditions mentioned above. [b] Isolated yields.

even with the prolonged reaction time when **2d** was employed. Steric effects of the methyl group on the double-bond carbon may be responsible for this negative result.

Conclusions

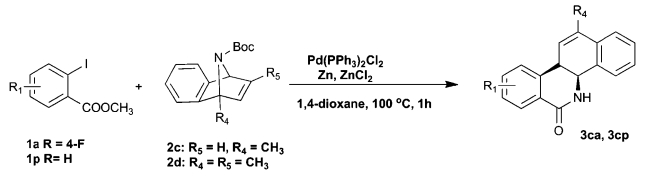
In summary, we have developed an improved and generally applicable base-free methodology for the annulation reaction of azabicyclic alkenes with substituted methyl *o*-halobenzoates. The present strategy provides an efficient construction of benzo[*c*]phenanthridine nucleus from readily available starting materials. Besides, high regioselectivity product is achieved when non-symmetric azabicyclic alkene is tested. Our process has shown broad functional group compatibility, which suggests that the method may be applied in the functionalized synthesis of both fully aromatized-type and partially hydrogenated-type alkaloids. Additional studies with regard to the enantioselectivity of this annulation reaction are currently under investigation in our lab and will be reported in due course.

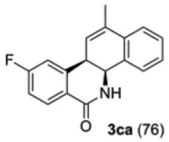
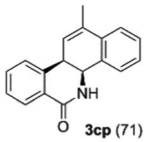
Experimental section

General remarks

Unless otherwise stated, all reactions were carried out under argon atmosphere, and all commercially available reagents were used without further purification. Tetrahydrofuran,

Table 5 Investigation of the regioselectivity of this annulation reaction[a]



Entry	Methyl *o*-iodobenzoate	Azabicycle	Product (yield %)[b]
1	**1a**	**2c**	 **3ca** (76)
2	**1p**	**2c**	 **3cp** (71)
3	**1p**	**2d**	No reaction

[a] All reactions were carried out under the optimal conditions. [b] Isolated yields.

acetonitrile, DMF, toluene, and 1,4-dioxane were purified by distillation under N_2 from Na/benzophenone immediately prior to use. IR spectra were recorded as thin films or KBr discs. NMR spectra were recorded with a spectrometer using $CDCl_3$. Chemical shifts (δ) were reported in parts per million (ppm) relative to either a tetramethylsilane internal standard or solvent signals. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiple), dd (doublet of doublet). Coupling constants were reported in Hertz (Hz). The melting points were determined and uncorrected. High-resolution mass spectra were conducted using an Ionspec 7.0T spectrometer by ESI-FTICR technique. Substrates **1b**[19], **1c**[20], **1d**[21], **1f**[1b], **1g**[22], **1h**[23], **1i**[24], **1q**[25], **1y**[26], **2a**[16], **2b**[17] and **2d**[27] are known compounds in literatures and analytical data was similar to what has been reported.

General procedure for the synthesis of methyl *o*-iodobenzoic acid[28]

substituted anthranilic acid (10 mmol) is suspended in a mixture of concentrated HCl (5 ml) and water (15 mL), cooled to 0 °C and stirred. Sodium nitrite (0.83 g, 12 mmol) dissolved in water (5 ml) is slowly added taking care to maintain the reaction temperature below 5 °C. Stirring is continued at 0 °C for 30 min. Potassium iodide (3.32 g, 20 mmol) is dissolved in a mixture of concentrated H_2SO_4 (0.6 ml) and water (5 ml) and added dropwise to the reaction mixture while keeping the reaction temperature below 10 °C. The mixture is then heated to 90 °C and stirred for 1 h, then cooled in an ice bath. The solid which separated was filtered, dissolved in ether (20 mL), and washed with 20% aqueous thiosulfate solution (3 × 15 mL). The organic layer was dried ($MgSO_4$) and evaporated to dryness under reduced pressure. The solid residue was recrystallized from water and dried *in vacuo* to afford methyl *o*-iodobenzoic acid.

General procedure for the synthesis of methyl *o*-halobenzoates

to a stirred solution of methyl *o*-halobenzoic acid (10 mmol) in CH_2Cl_2 (50 mL), oxalyl chloride (5.08 g, 20 mmol) was added, drops of DMF was added to catalyze the forming of benzoyl chloride. The mixture was stirred 2 h, then the solvent and excess oxalyl chloride was removed under reduce pressure and 30 mL of methanol was added to the residue in CH_2Cl_2 (30 mL). After the solution was stirred 30 min, saturated sodium bicarbonate (30 mL) was added and extracted, followed by drying over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatographic on silica gel with petroleum ether/ethyl acetate to afford the methyl *o*-halobenzoates.

4-Fluoro-2-iodobenzoate (1a)

2.66 g (95% yield), colorless liquid; IR (KBr): ν = 1733 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (m, 1H), 7.78–7.68 (m, 1H), 7.19–7.07 (m, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 164.8, 162.2, 132.8, 132.7, 128.8, 128.6, 115.3, 115.1, 94.61, 52.54 (extra peaks due to ^{13}C-^{19}F coupling); HRMS *m*/*z* calcd for $C_8H_6FIO_2$ $[M + H]^+$ 280.9475, found 280.9472.

3-Chloro-2-iodobenzoate(1e)

2.63 g (89% yield), colorless liquid; IR (KBr): ν = 1731 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (dd, J = 7.9, 1.5 Hz, 1H), 7.47 (dd, J = 7.7, 1.5 Hz, 1H), 7.35 (t, J = 7.8 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 140.8, 140.3, 131.4, 129.1, 127.6, 98.1, 52.9; HRMS *m*/*z* calcd for $C_8H_6ClIO_2$ $[M + H]^+$ 296.9174, found 296.9177.

5-Trifluoromethoxy-2-iodobenzoate (1k)

3.08 g (89% yield), colorless liquid; IR(KBr): ν = 1738 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 8.6 Hz, 1H), 7.71 (d, J = 2.6 Hz, 1H), 7.15–7.02 (m, 1H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 148.0, 141.8, 135.5, 124.2, 122.63, 120.5, 90.12, 51.83; HRMS *m*/*z* calcd for $C_9H_6F_3IO_3$ $[M + H]^+$ 346.9386, found 346.9380.

4-Trifluoromethyl-2-iodobenzoate(1l)

3.14 g (95% yield), colorless liquid; IR (KBr): ν = 1737 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.66–7.49 (m, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 137.6, 137.0, 133.2, 132.9, 129.9, 123.9 (q), 122.7, 119.98, 92.68, 51.85 (extra peaks due to ^{13}C–^{19}F coupling); HRMS *m*/*z* calcd for $C_9H_6F_3IO_2$ $[M + H]^+$ 330.9437, found 330.9437.

3-Trifluoromethyl-2-iodobenzoate (1m)

3.0 g (91% yield), colorless liquid; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 7.8 Hz, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.43 (t, J = 7.8 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 142.2, 131.7, 129.1(q), 128.1, 123.9, 121.4, 89.9, 53.0 (extra peaks due to ^{13}C–^{19}F coupling); IR (KBr): ν = 1737 cm^{-1} (C=O); HRMS *m*/*z* calcd for $C_9H_6F_3IO_2$ $[M + H]^+$ 330.9437, found 330.9436.

5-Amino-2-iodobenzoate (1n)[29]

To a stirred solution of **1q** (0.6 g, 2 mmol) in EtOH (10 ml), concentrated HCl (10 ml) was added and then tin(II) chloride dehydrate (1.8 g, 8 mmol) in EtOH(10 ml) was added dropwise. The mixture was stirred overnight at room temperature and white suspension appeared. Pour the mixture into water (50 ml) and adjust the pH to 11 by adding 2N NaOH solution, extracted with Et_2O (3 × 50 ml), washed with saturated brine (50 ml), dried over $MgSO_4$ and evaporated to give **1n** as a yellow oil (0.65 g, 85%). IR (KBr): ν = 3375 cm^{-1} (NH_2), 1722 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.5 Hz, 1H), 7.15 (d, J = 2.9 Hz, 1H), 6.52 (dd, J = 8.5, 2.9 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 146.4, 141.6, 135.6, 119.6, 117.5, 78.7, 52.4; HRMS m/z calcd for $C_8H_8INO_2$ $[M + H]^+$ 277.9672, found 277.9670.

5-*N*,*N*-Dimethyl-2-iodobenzoate (1o)[30]

To a solution of **1n** (0.55 g, 2 mmol) in *N*,*N*-dimethyl formamide (30 mL) was added K_2CO_3 (0.56 g, 4 mmol) and methyl iodide (0.85 g, 6 mmol). The solution was stirred overnight, poured into water and extracted with ethyl acetate. The organic phase was dried with anhydrous Na_2SO_4, filtered and removed by rotary evaporation to yield a residue. The residue was purified by column chromatography on silica gel and afforded **1o** as a yellow oil (0.53 g, 87%). IR (KBr): ν = 1730 cm^{-1}(C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.8 Hz, 1H), 7.11 (d, J = 3.1 Hz, 1H), 6.52 (dd, J = 8.8, 3.1 Hz, 1H), 3.92 (s, 3H), 2.96 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 149.9, 141.1, 135.5, 116.8, 114.7, 76.3, 52.4, 40.3; HRMS m/z calcd for $C_{10}H_{12}INO_2$ $[M + H]^+$ 305.9985, found 305.9989.

Preparation and data for 2c

Prepared according to the method of Carpino *et al.* from *o*-bromofluorobenzene and *N*-Boc-pyrrole in the presence of magnesium[31]. Magnesium turnings (136 mg, 5.5 mmol) were added to dry THF (5 mL) under argon and stirred with 1,2-dibromoethane (30 μl) for 10 min to activate Mg. After initiation, as evidenced by warming, a solution of *N*-Boc-2-methylpyrrole (0.91 g, 5 mmol) in THF (8 mL) was added and the mixture heated to reflux. Through the addition funnel, *ca.* one-fourth of a solution of *o*-bromofluorobenzene (0.9 g, 5 mmol) in THF (5 mL) was introduced. When initiation occurred, the rest of the solution was added dropwise. After the addition was complete the mixture was allowed to reflux for a further 1 h. It was then allowed to cool, quenched with a solution of NH_4Cl (3.0 g) in water (10 mL) and the organic layer extracted with diethyl ether (3 × 25 mL), dried and the solvent removed at reduced pressure. The residue was purified by column chromatography on silica gel and afforded **2c** as a white solid (0.71 g, 55%). Mp 80–82 °C; IR (KBr): ν = 1662 cm^{-1}(C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08–8.00 (m, 1H), 7.98–7.89 (m, 1H), 7.74 (s, 1H), 7.62–7.51 (m, 2H), 7.32 (d, J = 7.6 Hz, 1H), 6.79 (s, 1H), 2.69 (s, 3H), 1.59 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 132.0, 130.2, 130.0, 126.2, 125.4, 124.7, 123.9, 120.2, 118.3, 79.4, 27.4, 18.2, HRMS m/z calcd for $C_{16}H_{19}NO_2$ $[M + H]^+$ 258.1490, found 258.1493.

Typical procedure for the annulation reactions of azabicyclic alkenes with *o*-halobenzoates

To a solution of methyl *o*-halobenzoates **1** (1 mmol) in 1,4-dioxane (10 ml), azabicycle **2** (1.2 mmol), $Pd(PPh_3)_2Cl_2$(0.05 mmol, 28 mg), zinc powder (10 mmol, 0.75 g), and zinc chloride (0.5 mmol, 68 mg) were added. The mixture was then heated at 100 °C (**1j** at 60 °C) under N_2 atmosphere. After iodo ester disappeared (monitored by TLC), the reaction mixture was cooled, diluted with methylene chloride (15 mL). Then it was filtered through a short pad of Celite silica gel and washed with CH_2Cl_2 several times. After concentration *in vacuo*, the crude product was purified by silica gel column using ethyl acetate/petroleum ether as the eluent to give the corresponding *cis*-dihydrobenzo[*c*]phenanthridin-6-ones.

9-Fluoro-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3aa)

246 mg (93% yield), white solid, Mp176–178 °C; IR (KBr): ν = 1667 cm^{-1}(C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, J = 8.5, 5.9 Hz, 1H), 7.33 (dd, J = 15.2, 7.2 Hz, 3H), 7.19 (d, J = 7.2 Hz, 1H), 7.06 (dd, J = 20.1, 5.5 Hz, 2H), 6.65 (dd, J = 9.5, 2.0 Hz, 1H), 5.94 (s, 1H), 5.86 (dd, J = 9.5, 3.1 Hz, 1H), 4.91 (d, J = 5.6 Hz, 1H), 3.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.81, 164.32, 164.29, 142.59, 142.50, 132.6, 132.0, 130.9, 130.8, 129.3, 128.5, 127.9, 127.5, 127.4, 127.2, 124.5, 115.0, 114.8, 114.1, 113.8, 52.3, 38.6 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcdfor $C_{17}H_{12}NFO$ $[M + H]^+$ 266.0976, found 266.0975.

By-products 4aa

White solid, Mp 304–306 °C; IR (KBr): ν = 1665 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.33–8.03 (m, 1H), 7.59–6.97 (m, 6H), 6.44 (d, J = 45.6 Hz, 2H), 5.44 (s, 1H), 3.99–3.47 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.83, 164.53, 164.32, 140.1, 132.2, 128.8, 128.2, 127.5, 125.6, 124.2, 123.6, 115.7, 115.5, 112.2, 109.9, 50.3, 31.6 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{17}H_{12}NFO$ $[M + H]^+$ 266.0976, found 266.0973.

By-products 5aa

White solid, Mp 239–241 °C, IR (KBr): ν = 1660 cm^{-1}(C=O); ^1H NMR(400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.51 (s, 1H), 7.66 (s, 1H), 7.42–7.21 (m, 5H), 2.96 (m, 4H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 167.2, 137.3, 133.5, 131.3, 129.3, 128.5, 127.4, 121.3, 115.1 , 114.8, 110.9, 108.3, 108.1, 29.7, 21.6 (extra peaks due to ^{13}C-^{19}F coupling); HRMS m/z calcd for $C_{17}H_{12}NFO$ $[M + H]^+$ 266.0976, found 266.0971.

10-Fluoro-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ab)

199 mg (75% yield), white solid, Mp178–180 °C; IR (KBr): ν = 1641 cm^{-1}(C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.7 Hz, 1H), 7.55–7.12 (m, 7H), 6.63 (dd, J = 9.5, 2.8 Hz, 1H), 5.69 (d, J = 9.5 Hz, 1H), 5.42 (s, 1H), 4.85 (d, J = 5.3 Hz, 1H), 4.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 160.6, 158.2, 132.68, 131.0,129.8, 128.7, 128.7, 128.4, 128.3, 127.4, 127.3, 126.6, 126.5, 123.9, 119.7, 119.5, 51.8, 32.9 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{17}H_{12}NFO$ $[M + H]^+$ 266.0976, found 266.0974.

8-Fluoro-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ac)

246 mg (93% yield), white solid, Mp 222–225 °C; IR (KBr): ν = 1670 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.89–7.73 (m,

1H), 7.46–7.14 (m, 6H), 6.75–6.52 (m, 1H), 5.98–5.56 (m, 2H), 4.88 (d, J = 5.6 Hz, 1H), 3.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 163.5, 161.0, 135.3, 132.6, 131.7, 129.5, 129.0, 128.5, 128.3, 127.6, 127.5, 127.2, 120.2, 120.0, 114.8, 114.6, 52.4, 38.1 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{17}H_{12}NFO$ $[M + H]^+$ 266.0976, found 266.0975.

9-Chloro-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ad)

261 mg (93% yield), white solid, Mp 202–204 °C; IR (KBr): ν = 1666 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.3 Hz, 1H), 7.47–7.25 (m, 5H), 7.18 (d, J = 7.2 Hz, 1H), 6.64 (dd, J = 9.6, 2.3 Hz, 1H), 6.01 (s, 1H), 5.85 (dd, J = 9.5, 3.1 Hz, 1H), 4.89 (d, J = 5.5 Hz, 1H), 3.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 141.4, 139.0, 132.5, 132.0, 129.6, 129.3, 128.5, 128.0, 128.0, 127.5, 127.4, 127.2, 127.1, 126.6, 52.2, 38.4; HRMS m/z calcd for $C_{17}H_{12}NClO$ $[M + H]^+$ 282.0680, found 282.0675.

10-Chloro-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ae)

211 mg (71% yield), white solid, Mp 182–184 °C; IR (KBr): ν = 1666 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.38 (dd, J = 10.1, 5.5 Hz, 2H), 7.35–7.20 (m, 3H), 6.63 (dd, J = 9.5, 2.9 Hz, 1H), 5.65 (d, J = 9.5 Hz, 1H), 5.37 (s, 1H), 4.82 (d, J = 5.1 Hz, 1H), 4.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 137.0, 133.6, 132.9, 132.8, 130.9, 129.9, 129.9, 128.6, 128.4, 128.4, 127.6, 127.4, 126.9, 126.9, 51.7, 36.7; HRMS m/z calcd for $C_{17}H_{12}NClO$ $[M + H]^+$ 282.0680, found 282.0680.

8-Chloro-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3af)

253 mg (90% yield), white solid, Mp 219–221 °C; IR (KBr): ν = 1672 cm^{-1}(C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.84–7.63 (m, 2H), 7.63–7.47 (m, 3H), 7.20 (d, J = 7.3 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 5.91–5.64 (m, 2H), 4.89 (d, J = 5.3 Hz, 1H), 4.34 (t, J = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 137.9, 133.9, 133.0, 132.6, 131.7, 130.9, 129.5, 128.7, 128.6, 128.1, 127.9, 127.7, 127.5, 127.3, 52.2, 38.2; HRMS m/z calcd for $C_{17}H_{12}NClO$ $[M + H]^+$ 282.0680, found 282.0684.

10-Methyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ag)

222 mg (85% yield), white solid, Mp 201–203 °C; IR (KBr): ν = 1660 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 1H), 7.48–7.12 (m, 6H), 6.62 (dd, J = 9.5, 3.1 Hz, 1H), 5.59 (d, J = 9.5 Hz, 1H), 5.30 (s, 1H), 4.77 (d, J = 5.2 Hz, 1H), 4.03 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 137.6, 135.0, 134.7, 132.8, 131.6, 129.7, 128.4, 128.3, 128.0, 127.7, 127.5, 127.3, 127.3, 126.2, 51.9, 35.9, HRMS m/z calcd for $C_{18}H_{15}NO$ $[M + H]^+$ 262.1226, found 262.1229.

8-Methyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ah)

245 mg (94% yield), white solid, Mp 196–198 °C; IR (KBr): ν = 1669 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.37–7.17 (m, 5H), 6.56 (dd, J = 9.6, 2.6 Hz, 1H), 5.79 (dd, J = 9.5, 2.7 Hz, 1H), 5.67 (s, 1H), 4.84 (d, J = 5.7 Hz, 1H), 3.96–3.72 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.33, 137.50, 136.61, 133.80, 132.75, 132.09, 129.26, 128.92, 128.37, 128.32, 127.76, 127.59, 127.18, 127.09, 127.06, 52.36, 38.34, 21.08; HRMS m/z calcd for $C_{18}H_{15}NO$ $[M + H]^+$ 262.1226, found 262.1228.

8-Methoxy-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ai)

263 mg (95% yield), white solid, Mp182–184 °C; IR (KBr): ν = 1668 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 2.7 Hz, 1H), 7.38–7.05 (m, 6H), 6.56 (dd, J = 9.6, 2.5 Hz, 1H), 5.77 (dd, J = 9.5, 2.5 Hz, 1H), 5.62 (s, 1H), 4.84 (d, J = 5.6 Hz, 1H), 3.85 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 159.2, 132.8, 132.0, 131.6, 129.3, 129.0, 128.4, 128.3, 127.6, 127.1, 127.1, 55.6, 52.5, 38.0; HRMS m/z calcd for $C_{18}H_{15}NO_2$ $[M + H]^+$ 278.1176, found 278.1177.

8-Bromo-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3aj)

279 mg (86% yield), white solid, Mp 243–245 °C; IR (KBr): ν = 1664 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 2.0 Hz, 1H), 7.58 (dd, J = 8.1, 2.1 Hz, 1H), 7.37–7.02 (m, 6H), 6.53 (dd, J = 9.6, 2.5 Hz, 1H), 5.70 (dd, J = 9.5, 2.8 Hz, 1H), 5.46 (s, 1H), 4.79 (d, J = 5.6 Hz, 1H), 3.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 137.4, 134.9, 131.5,130.6, 129.9, 128.8, 128.5, 127.9, 127.5, 126.8, 126.7, 126.5, 126.3, 120.6, 51.2, 37.2, HRMS m/z calcd for $C_{17}H_{12}BrNO$ $[M + H]^+$ 326.0175, found 326.0175.

8-trifluoromethoxy-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ak)

301 mg (91% yield), white solid, Mp 174–176 °C; IR (KBr): ν = 1676 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.41–7.24 (m, 5H), 7.18 (d, J = 7.3 Hz, 1H), 6.61 (dd, J = 9.6, 2.4 Hz, 1H), 5.95–5.67 (m, 2H), 4.88 (d, J = 5.6 Hz, 1H), 3.92 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 148.7, 138.2, 132.5, 131.6, 129.9, 129.5, 128.9, 128.6, 127.8, 127.6, 127.3, 125.5, 124.3, 121.7, 120.4, 52.2, 38.2 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{18}H_{12}F_3NO_2$ $[M + H]^+$ 332.0893, found 332.0895.

9-Trifluoromethyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3al)

283 mg (90% yield), white solid, Mp 211–213 °C; IR (KBr): ν = 1668 cm^{-1} (C=O); ^{1}H NMR (400 MHz, CDCl3) δ 8.19 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 21.9 Hz, 1H), 7.44–7.21 (m, 3H), 7.18 (d, J = 7.2 Hz, 1H), 6.64 (dd, J = 9.6, 2.4 Hz, 1H), 6.03 (s, 1H), 5.84 (dd, J = 9.5, 3.0 Hz, 1H), 4.91 (d, J = 5.7 Hz, 1H), 3.96 (m, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 163.8, 140.5, 134.6, 134.3, 132.5, 131.7, 131.2, 129.5,128.7, 128.1, 128.1, 127.5, 127.3, 125.0, 124.62–124.51(m), 124.19–124.09 (m), 124.2, 122.2, 52.2, 38.5 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{18}H_{12}F_3NO$ $[M + H]^+$ 316.0944, found 316.0941.

10-Trifluoromethyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3am)

224 mg (71% yield), white solid, Mp 236–238 °C; IR (KBr): ν = 1665 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 7.7 Hz, 1H), 7.91 (d, J = 7.8 Hz, 1H), 7.56 (t, J = 7.9 Hz, 1H), 7.47–7.37 (m, 1H), 7.37–7.19 (m, 3H), 6.61 (dd, J = 9.5, 3.0 Hz, 1H), 5.63 (d, J = 9.6 Hz, 1H), 5.44 (s, 1H), 4.80 (d, J = 4.3 Hz, 1H), 4.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 138.2, 132.6, 132.1, 130.8, 130.4–130.2 (m), 130.0, 129.9, 128.5, 128.3, 128.2, 127.9, 127.8, 127.4, 127.1, 125.4, 52.1, 36.4 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{18}H_{12}F_3NO$ $[M + H]^+$ 316.0944, found 316.0942.

8-Amino-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3an)

238 mg (91% yield), white solid, Mp 103–105 °C; IR (KBr): ν = 1661 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, J = 2.6 Hz, 1H), 7.35–7.21 (m, 3H), 7.12 (dd, J = 20.6, 7.7 Hz, 2H), 6.84 (dd, J = 8.1, 2.6 Hz, 1H), 6.54 (dd, J = 9.6, 2.6 Hz, 1H), 5.76 (dd, J = 9.5, 2.6 Hz, 1H), 5.60 (s, 1H), 4.81 (d, J = 5.7 Hz, 1H), 3.79 (dd, J = 5.5, 2.7 Hz, 2H), 3.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 146.0, 132.8, 132.2, 129.6, 129.2, 129.2, 128.7, 128.22, 128.1, 127.6, 127.0, 126.9, 119.7, 113.8, 52.5, 38.0; HRMS m/z calcd for $C_{17}H_{14}N_2O$ $[M + H]^+$ 263.1179, found 263.1181.

8-*N*,*N*-Dimethyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ao)

264 mg (91% yield), white solid, Mp 241–243 °C; IR (KBr): ν = 1660 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78–7.62 (m, 1H), 7.58–7.42 (m, 2H), 7.36–7.25 (m, 3H), 7.20–7.05 (m, 2H), 6.90 (dd, J = 8.4, 2.8 Hz, 1H), 6.53 (dd, J = 9.6, 2.6 Hz, 1H), 5.77 (dd, J = 9.5, 2.4 Hz, 1H), 5.49 (s, 1H), 4.81 (d, J = 5.6 Hz, 1H), 3.88–3.75 (m, 1H), 2.99 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 150.1, 132.9, 132.2, 129.8, 129.2, 128.6, 128.2, 127.9, 127.7, 127.0, 126.9, 126.9, 117.1, 111.3, 52.6, 40.7, 37.9; HRMS m/z calcd for $C_{19}H_{18}N_2O$ $[M + H]^+$ 291.1492, found 291.1496.

13,14-*cis*-Dihydrobenzo[*c*]phenanthridin-6-one (3ap)

227 mg (92% yield), white solid, Mp173–175 °C; IR (KBr): ν = 1657 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 7.7, 1.1 Hz, 1H), 7.53 (td, J = 7.5, 1.4 Hz, 1H), 7.39 (td, J = 7.6, 1.0 Hz, 1H), 7.36–7.25 (m, 4H), 7.16 (d, J = 7.2 Hz, 1H), 6.58 (dd, J = 9.6, 2.7 Hz, 1H), 5.80 (dd, J = 9.6, 2.7 Hz, 1H), 5.76 (s, 1H), 4.87 (d, J = 5.7 Hz, 1H), 3.89 (dt, J = 5.4, 2.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 139.6, 133.0, 132.7, 132.0, 129.3, 128.6, 128.4, 128.0, 128.0, 127.7, 127.62, 127.29, 127.13, 127.1, 52.2, 38.7; HRMS m/z calcd for $C_{17}H_{13}NO$ $[M + H]^+$ 248.1070, found 248.1074.

8-Trifluoromethyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ax)

290 mg (92% yield), white solid, Mp 175–177 °C; IR (KBr): ν = 1661 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.72 (dd, J = 8.0, 1.4 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.25 (m, 3H), 7.15–7.05 (m, 1H), 6.91 (s, 1H), 6.57 (dd, J = 9.6, 2.4 Hz, 1H), 5.74 (dd, J = 9.6, 3.3 Hz, 1H), 4.87 (d, J = 5.1 Hz, 1H), 3.97–3.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 142.5, 131.3, 129.7, 129.6, 129.1, 128.6, 127.9, 127.5, 126.9, 126.8, 126.5, 126.3, 125.5, 124.4, 51.2, 36.9 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{18}H_{12}F_3NO$ $[M + H]^+$ 316.0944, found 316.0943.

8,9-Methylenedioxy-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ay)

274 mg (94% yield), white solid, Mp 227–230 °C; IR (KBr): ν = 1655 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.30–7.19 (m, 3H), 7.09 (d, J = 7.3 Hz, 1H), 6.67 (s, 1H), 6.51 (dd, J = 9.6, 2.6 Hz, 1H), 5.96 (dd, J = 6.9, 1.3 Hz, 2H), 5.69 (dd, J = 9.5, 2.5 Hz, 1H), 5.43 (s, 1H), 4.75 (d, J = 5.7 Hz, 1H), 3.81–3.62 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 150.3, 146.3, 134.1, 131.7, 130.8, 128.3, 127.3, 127.3, 126.5, 126.3, 126.1, 121.1, 106.9, 106.0, 100.7, 51.3, 37.4; HRMS m/z calcd for $C_{18}H_{13}NO_3$ $[M + H]^+$ 292.0968, found 292.0967.

8,9-Dimethoxy-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3az)

292 mg (95% yield), white solid, Mp 238–241 °C; IR (KBr): ν = 1672 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.37 (s, 1H), 7.26–7.18 (m, 2H), 7.14 (m, 1H), 7.04 (d, J = 7.4 Hz, 1H), 6.66 (s, 1H), 6.49 (dd, J = 9.6, 2.3 Hz, 1H), 5.70 (dd, J = 9.6, 3.3 Hz, 1H), 4.79 (d, J = 6.3 Hz, 1H), 3.88 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 153.3, 147.6, 132.8, 131.3, 129.4, 128.5, 127.8, 127.1, 126.7, 126.0, 125.9, 117.1, 109.6, 108.1, 55.2, 51.7, 36.1; HRMS m/z calcd for $C_{19}H_{17}NO_3$ $[M + H]^+$ 308.1281, found 308.1285.

9-Fluoro-13,14-*cis*-dihydrobenzodioxole benzo[*c*]phenanthridin-6-one (3ba)

290 mg (94% yield), white solid, Mp 230–233 °C; IR (KBr): ν = 1665 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 (m, 1H), 7.05–6.89 (m, 2H), 6.72 (s, 1H), 6.59 (s, 1H), 6.41 (dd, J = 9.5, 2.3, 1H), 5.90 (d, J = 2.8, 2H), 5.78 (s, 1H), 5.64 (dd, J = 9.5, 3.0, 1H), 4.71 (d, J = 5.6, 1H), 3.83–3.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 163.4, 147.1, 146.4, 141.4, 129.9, 129.8, 126.6, 126.1, 124.7, 114.0, 113.8, 113.0, 112.8, 107.2, 106.8, 100.4, 51.4, 37.6 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{18}H_{12}FNO_3$ $[M + H]^+$ 310.0874, found 310.0871.

8-Fluoro-13,14-*cis*-dihydrobenzodioxole benzo[*c*]phenanthridin-6-one (3bc)

281 mg (91% yield), white solid, Mp 228–230 °C; IR (KBr): ν = 1667 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.82–7.53 (m, 2H), 7.37–7.13 (m, 2H), 6.77 (s, 1H), 6.67 (s, 1H), 6.46 (dd, J = 9.5, 2.3 Hz, 1H), 5.98 (m, 2H), 4.75 (d, J = 5.5 Hz, 1H), 3.83 (s, 1H); ^{13}C NMR(100 MHz, $CDCl_3$) δ 163.2, 147.4, 135.8, 130.9, 128.9, 127.2, 126.6, 125.9, 120.3, 120.1, 114.9, 114.8, 108.5, 107.8, 101.4, 52.5, 38.2 (extra peaks due to ^{13}C–^{19}F coupling); HRMS m/z calcd for $C_{18}H_{12}FNO_3$ $[M + H]^+$ 310.0874, found 310.0874.

9-Chloro-13,14-*cis*-dihydrobenzodioxole benzo[*c*]phenanthridin-6-one (3ba)

293 mg (90% yield), white solid, Mp 206–209 °C; IR (KBr): ν = 1671 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.93 (m, 1H), 7.26 (m, 2H), 6.73 (s, 1H), 6.60 (s, 1H), 6.43 (dd, J = 9.5, 2.1, 1H), 5.98 (s, 1H), 5.91 (d, J = 3.1, 2H), 5.66 (dd, J = 9.5, 3.0, 1H), 4.71 (d, J = 5.6, 1H), 3.86–3.69 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 148.1, 147.5, 141.5, 139.1, 129.6, 128.1, 128.0, 128.0, 127.7, 127.1, 127.1, 126.4, 125.7, 108.3, 107.8, 101.4, 52.4, 38.3; HRMS m/z calcd for $C_{18}H_{12}ClNO_3$ $[M + H]^+$ 326.0578, found 326.0577

8-Methoxy-13,14-*cis*-dihydrobenzodioxole benzo[*c*]phenanthridin-6-one (3bi)

302 mg (94% yield), white solid, Mp 232–234 °C; IR (KBr): ν = 1678 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71–7.63 (m, 1H), 7.55–7.46 (m, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.08 (dd, J = 8.3, 2.8 Hz, 1H), 6.77 (s, 1H), 6.66 (s, 1H), 6.43 (dd, J = 9.6, 2.6 Hz, 1H), 5.98 (d, J = 1.2 Hz, 2H), 5.66 (dd, J = 9.5, 2.5 Hz, 1H), 5.54 (s, 1H), 4.74 (d, J = 5.7 Hz, 1H), 3.86 (s, 3H), 3.83–3.72 (m, 1H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 159.2, 147.3, 132.2, 132.1, 130.9, 128.8, 128.3, 127.3, 126.8, 120.6, 111.1, 108.4, 107.7, 101.5, 65.2, 52.7, 38.3; HRMS *m*/*z* calcd for $C_{19}H_{15}NO_4$ $[M + H]^+$ 322.1074, found 322.1076.

8-Trifluoromethoxy-13,14-*cis*-dihydrobenzodioxole benzo[*c*]phenanthridin-6-one (3bk)

341 mg (91% yield), white solid, Mp 192–196 °C; IR (KBr): ν = 1680 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 (s, 1H), 7.38 (s, 2H), 6.82 (s, 1H), 6.68 (s, 1H), 6.50 (dd, *J* = 9.6, 2.3, 1H), 6.35 (s, 1H), 5.99 (d, *J* = 4.8, 2H), 5.70 (dd, *J* = 9.5, 2.8, 1H), 5.32 (s, 1H), 4.81 (d, *J* = 5.7, 1H), 3.96–3.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 147.7, 147.2, 146.5, 137.3, 132.0, 131.6, 131.5, 128.47, 127.9, 127.8, 126.6, 126.1, 124.68, 124.66, 124.1, 120.7, 119.4, 107.4, 106.8, 100.4, 51.5, 36.9 (extra peaks due to ^{13}C–^{19}F coupling); HRMS *m*/*z* calcd for $C_{19}H_{12}F_3NO_4$ $[M + H]^+$ 376.0791, found 376.0791.

8-Trifluoromethyl-13,14-*cis*-dihydrobenzodioxole benzo[*c*]phenanthridin-6-one (3bx)

334 mg (93% yield), white solid, Mp 238–240 °C; IR (KBr): ν = 1683 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.90–7.35 (m, 3H), 6.76 (d, *J* = 41.9, 1H), 6.52 (s, 1H), 6.01 (s, 1H), 5.71 (s, 2H), 4.82 (s, 1H), 3.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 147.2, 146.5, 142.5, 131.1, 131.0, 130.9, 128.4, 127.7, 127.5, 127.4, 127.2, 126.8, 126.7, 126.1, 124.5, 124.2, 107.3, 106.9, 100.5, 51.3, 37.6 (extra peaks due to ^{13}C–^{19}F coupling); HRMS *m*/*z* calcd for $C_{19}H_{12}F_3NO_3$ $[M + H]^+$ 360.0842, found 360.0841.

9-Fluoro-12-methyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3ca)

212 mg (76% yield), white solid, Mp 213–215 °C; IR (KBr): ν = 1660 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 2.5 Hz, 1H), 7.35–7.26 (m, 2H), 7.20 (d, *J* = 10.6 Hz, 2H), 7.03–6.88 (m, 2H), 5.93 (s, 1H), 5.54 (s, 1H), 4.77 (d, *J* = 5.6 Hz, 1H), 3.77 (s, 1H), 2.03 (s, 3H); ^{13}CNMR (100 MHz, $CDCl_3$) δ 165.2, 163.0, 162.6, 141.5, 141.4, 132.5, 131.1, 130.5, 129.2, 129.1, 127.6, 127.1, 126.6, 125.7, 122.3, 122.1, 113.2, 113.0, 112.4, 112.2, 50.9, 36.6, 28.0 (extra peaks due to ^{13}C–^{19}F coupling); HRMS *m*/*z* calcd for $C_{18}H_{14}FNO$ $[M + H]^+$ 280.1132, found 280.1134.

12-Methyl-13,14-*cis*-dihydrobenzo[*c*]phenanthridin-6-one (3cp)

185 mg (71% yield), white solid, Mp 201–203 °C; IR (KBr): ν = 1664 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.3 Hz, 1H), 7.48–7.44 (m, 1H), 7.32–7.30 (m, 3H), 7.26–7.20 (m, 3H), 5.54–5.52 (m, 2H), 4.76 (d, *J* = 5.5 Hz, 1H), 3.82–3.76 (m, 1H), 2.06–2.01 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 139.2, 133.4, 132.0, 131.3, 131.0, 129.9, 128.3, 127.8, 127.1, 127.0, 126.6, 126.2, 124.2, 122.9, 51.6, 37.6, 28.7; HRMS *m*/*z* calcd for $C_{18}H_{15}NO$ $[M + H]^+$ 262.1226, found 262.1229.

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